The Pentagon funds 80 percent of this research in the United States, and some of these researchers fear that the Pentagon, in its drive for widespread acceptance of Ada, will decide that anybody who does computer research for the Pentagon will have to use Ada. This, say the researchers, would inhibit creativity. "Some Pentagon people have a naive belief that if the research was done in this language it would be easier to apply," says Jerome A. Feldman, chairman of computer science at the University of Rochester. "That's silly."

To fend off this possibility, these researchers asked the Defense Advanced Research Projects Agency (DARPA) to study whether the use of Ada by the artificial intelligence research community was feasible. The study, performed by DARPA by SRI International, concluded that it was not. "We cut them off before it became an issue," says Feldman. Other areas may be affected, however, since there will be more academic support for Ada-related research than for all other such research combined. "To some extent that will have tremendously good effects," says Feldman. "But to the extent that these requirements are different than other ones, it may bias that whole line of work. Ada is a large, high-momentum object stuck into this research system. And its ramifications are going to continue to spread throughout computer science, for better or worse."

It remains to be seen whether the Pentagon's drive for language unification will be thwarted by academics, with their desire for freedom to choose which language to use for computer research, or by the Navy, with its apparent desire to keep secrets from the other services. If developments are similar to those described by the Biblical Patriarchs, the outlook for continued proliferation of computer languages is good.

—WILLIAM J. BROAD

The Complete Index to Man

There is a plan to catalog every protein produced in the human body; meanwhile DNA sequences accumulate apace

The complete understanding of man may remain a distant prospect, but a complete description in the language of molecular biology has suddenly begun to appear within the realm of possibility. A total analysis of the human genome, as well as an index of every protein produced by the various types of cell in the human body, are goals that through new techniques and advances in computing power have begun to appear almost feasible.

Neither goal is exactly around the corner. A total of some 350,000 DNA bases from the entire living kingdom had been reported in the scientific literature by December 1980, whereas a single human chromosome contains on the order of 500 million bases. Nonetheless, the power of the new rapid sequencing methods means that sizeable segments of the human genome can now be analyzed if the need arises.

Perhaps further off is the goal of identifying every protein made in the human body. Yet an ambitious project to do just that has already been devised. Its originators are two scientists at the Argonne National Laboratory, Norman G. Anderson and his son Leigh Anderson. Over the last few years they have laid much of the technical groundwork for cataloging the 50,000 or so different protein products that constitute the working parts of human cells.

A human protein index, in their view, would fulfill for molecular biology the role that sky maps do for astronomy or even the periodic table for chemistry. It represents the kind of systematic cataloging of basic subject matter which is the hallmark of a mature discipline.

"Only 300 to a thousand human proteins have been characterized in any reasonable detail—which is just a few percent of the number there. The alchemists knew a larger fraction of the atomic table," remarks Norman Anderson.

The Andersons' plan is simple in concept, technically arduous in design. Their intent is to identify each human protein by the coordinates of the position it takes up in a standard mapping system. The mapping system is a specialized version of the technique known as two-dimensional gel electrophoresis.

The proteins extracted from a particular human tissue are separated in one dimension according to their electric charge, and in a second dimension by their molecular weight. The result is a complex map, often of more than 1000 separable spots.

The Andersons' aim is to standardize the preparation and reading of the two-dimensional gels to such an extent that each human protein can be recognized by its map coordinates.

Construction of the human protein index would be no minor task. Asked recently by Senator Alan Cranston (D-Calif.) for the costs of a crash program to complete the index, the Andersons estimated that some $350 million would be needed over the next 5 years. Cranston became interested in the project through his attention to aging, nutrition, and biomedical research in general. The idea for a crash program seems now to have receded, but Cranston is still actively interested in the project and has a high-powered task force reporting to him on how the project should be supported. Funding on the order of $10 million a year seems to be the present objective. "This could be the basis for a major stimulus to the biotechnology industry in this country," remarks a Cranston aide, who says the senator plans to interest the Reagan Administration in the project.

> The human protein would reveal the pattern of cell development

What would justify a multimillion dollar budget, the Andersons believe, are the various potential applications of the human protein index, chiefly in diagnosing disease, measuring the human mutation rate, and assessing the genetic impact of environmental pollutants. They

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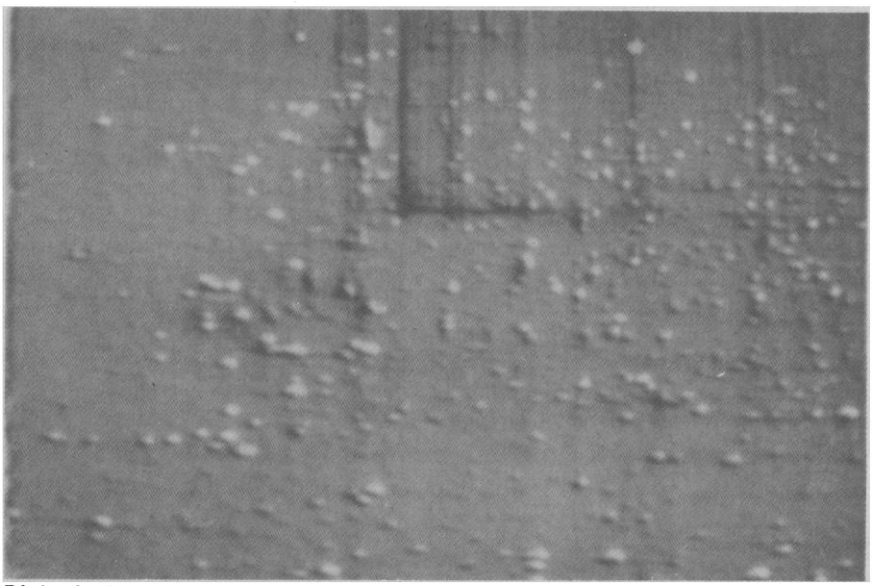

Biological star chart?

Two-dimensional gel map, prepared in the Anderson's laboratory, of normal human lymphocytes. Each spot represents a different protein.

hope that the index will be relevant to the understanding of cancer by showing what proteins are switched on or off in malignant cells. "It is unlikely that human cancer will be either understood or effectively cured without a complete list of all human protein gene products, and a schedule showing the order in which they appear during human development," the Andersons have written.

Not everyone is so enthusiastic about the project. For one thing, Apollo style programs have not been particularly successful in the biological sciences. For another, biologists might be expected to oppose any such program if it seems likely to be supported out of the part of the federal budget already earmarked for biological research. Then there are doubts as to whether the two-dimensional gel technique can be standardized faster than biological variability can move to defeat it.

The separation of proteins on gels is a laboratory technique of long standing. But recent refinements, notably those made in 1975 by Patrick O'Farrell, when he was a graduate student at the University of Colorado, have significantly increased the resolving power of the method. It is already being used to map the proteins produced by such organisms as *Escherichia coli*, yeast, and rodents.

The Andersons have gone straight to humans, primarily because of the diagnostic opportunities they see in the technique. Another reason is that Norman Anderson has, in a sense, had this goal in mind for at least 20 years. In 1959, while at the Oak Ridge National Laboratory, he conceived a plan to separate and characterize as completely as possible all the chemically definable constituents of human cells.

In pursuit of this goal he came up with the invention which has made him widely known to biologists, the zonal ultracentrifuge, now used throughout the world to produce, among other things, vaccines of high purity and minimum side effects. He also invented the centrifugal fast analyzer, an instrument widely used in clinical laboratories.

Now at the Argonne National Laboratory near Chicago, Anderson seized upon the two-dimensional gel technique as a way of realizing his original goal of human molecular anatomy. Leigh Anderson had returned from Cambridge where he studied under crystallographer Max Perutz, and together they set to developing the O'Farrell two-dimensional gel technique into a method suitable for large volume use.

With a 13-person team and a budget of around $1 million from Argonne, the Andersons are now able to run about 10,000 gels a year. Progress has also been made on writing computer programs whereby each spot on a two-dimensional gel map can be identified and measured. The group has already prepared protein maps of several human tissues, such as lymphocytes, muscle, plasma, and urine. Presaging the diagnostic potential of the technique, the Anderson team has noticed differences between the pattern of protein spots produced by normal and by malignant cells. The medical and commercial payoff, they believe, will come when the full index of all human proteins is available as a standard of comparison against which possibly diseased tissues can be judged.

The grand scheme calls not just for assignment of map coordinates to each protein spot but also for study of other properties. The Andersons have plans for measuring the quantity of each protein produced and identifying each spot with monoclonal antibodies. The objective is to describe each spot with enough detail that each human protein can be distinguished from all the rest, including from the products of allelic genes. Once the index is compiled, it would be made available on a computer tape or otherwise as a standard biological reference work.

"List-based biology, which this project makes possible," say the Andersons, "will be a science in itself, and will be concerned with the details of the organization of gene expression, . . . with misregulation in cancer, and with the details of genetic disease."

Another kind of list-making is that made possible by DNA sequences. Since the invention in 1977 of the two rapid methods for analyzing DNA sequences, data have been pouring out of laboratories in an ever increasing flood.

So far the only organisms whose entire genome has been sequenced are a handful of scientifically important small viruses, which are only 5000 bases or so in length. Rumor has it that the DNA both of human mitochondria and of bacteriophage lambda are at or near completion. The next major landmark will be the sequencing of the bacterium *Escherichia coli*, whose genome has around 5 million bases.

From *E. coli* to man is a long leap, but the European Molecular Biology Laboratory has been contemplating the possibility of sequencing one of the 46 human chromosomes, which contain around 500 million bases apiece.

The avalanche of DNA data has given rise to a proposal for a national nucleic acid sequence data bank. The National Institutes of Health (NIH) plans to let a contract early next year for founding such a center, and the European Molecular Biology Laboratory has similar ideas. The bank would probably be a collection of data together with the computers and programs to analyze the data, and would be accessible through telecommunications networks.

The most complete among several collections of DNA data is that maintained by Margaret Dayhoff and colleagues at the National Biomedical Research Foundation. Dayhoff is perhaps best known for her *Atlas of Protein Sequence and*

Structure, an ongoing compilation of protein sequence data. She has also collected DNA sequences, not least because they now often serve as the source for determining protein sequences. Other DNA bankers, however, have concentrated less on the collection of data from the literature, more on ways to manipulate it. Laurence Kedes and colleagues at Stanford University have established a computerized data system, accessible through telecommunications networks, which now has some 200 regular users from among the molecular genetics community. The intent of the NIH is to combine the advantages of both approaches in the national nucleic acid data bank.

The notion of cataloging every human protein or sequencing the entire human genome appeals to the sense of completeness. Both are doubtless worthy goals that will be attained sooner or later. Yet it would be a reductionist fallacy to suppose that even knowledge of the complete molecular anatomy of man will tell but a fraction of the story.

—NICHOLAS WADE

Dinosaur Battle Erupts in British Museum

Anti-cladist sees reds under fossil beds in alliance with creationists to subvert the Establishment

In the solemn halls of the British Museum of Natural History, where the curious come to gape at the bones of creatures long since extinct, the sounds of a rude contemporary fracas are perturbing the Cretaceous stillness.

What has jolted the fossils to life is the charge that the new arrangement in which they have been exhibited to the public conceals, or at least makes only subliminally manifest, a pernicious political doctrine.

The new exhibits, according to zoologist L. B. Halstead of the University of Reading, are designed to favor a Marxist view of the world at the expense of conservatism. Worse, they give comfort not just to Marxists but also to creationists, the Bible-packing fundamentalists who are always trying to lose the theory of evolution down a gap in the fossil record.

The authorities at the British Museum have elected to maintain a dignified silence in the face of these charges, which first appeared in a letter from Halstead to *Nature*. A museum scientist wrote to impart his view that Halstead was "simply mistaken," and there the matter rests.

The dinosaurs that constitute the bones of contention have been downgraded in their claim on exhibition space. But what has provoked Halstead to outrage is that they are displayed according to the principles of cladistics, a system of classifying relationships among objects. As an analytical tool, cladistics has been intensively used among paleontologists and evolutionary biologists for the last 10 years or so. For some, cladistics has become more of a creed than a tool. Like the reds and the greens in Byzantium, or the Guelfs and the Ghibellines in Dante's Italy, the cladists and their opponents have on occasion turned departments of paleontology into fields of passionate but obscure dispute. An early battle zone was the American Museum of Natural History in New York.

The cladist wars reached a peak of intensity in the mid-1970's, and have since subsided. What is new about Halstead's onslaught is his belief that cladism has a political dimension. Cladistics, in his view, leads to the assumption that evolution has not proceeded by gradual change, as envisaged by Darwin and his successors, but rather by sudden leaps and discontinuities. "If it could be established that the pattern of evolution was a saltatory one after all, then at long last the Marxists would indeed be able to claim that the theoretical basis of their approach was supported by scientific evidence. . . . What is going on at the Natural History Museum needs to be seen in context. If the cladistic approach becomes established as the received wisdom, then a fundamentally Marxist view of the history of life will have been incorporated into a key element of the educational system of this country," wrote Halstead in his letter to *Nature*.

"I think Halstead is completely mistaken," remarks museum paleontologist Colin Patterson. In Patterson's view, cladistics is not even about evolution: it is merely a tool for studying patterns and

Scherraine Mack

Can dinosaurs express political opinions?

This Triceratops, *caught midway between Congress and the White House, said it had been around Washington too long to care one way or the other.*

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